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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/641,327 | 08/18/2000 | Gregory E. Agoston | 05213-0730 (43170-219693) | 7032 |
| 23370 | 7590 | 12/16/2004 | EXAMINER | |
| JOHN S. PRATT, ESQ KILPATRICK STOCKTON, LLP 1100 PEACHTREE STREET ATLANTA, GA 30309 | | | QAZI, SABIHA NAIM | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1616 | |

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/641,327

Applicant(s)

AGOSTON ET AL.

Examiner

Sabiha Qazi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) _____ is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 13-16 and 18 is/are allowed.
- 6) ☐ Claim(s) 39, 12 and 17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/5/04 has been entered.

Claims 12-18 and 39 are pending.

Claims are drawn to method of inhibiting angiogenesis by 2-methoxy, 16-substitued estradiols.

Rejection under 35 U.S.C. 112, first paragraph, is withdrawn because claims are amended.

Prior art of record teaches method of treatment of angiogenesis, for example 2-methoxy estradiol, 2-ethoxy estradiol, 2-alkoxyestradiol derivatives, esterone, 2-hydroxyalkylestradiols, All the compounds are estradiol derivatives known to treat angiogenesis or cancer.

Data in the specification

On page 33, Table 2 shows the test data for the compounds 2-methylhydroxy-E2, (2ME2 is known), and other compounds having 2-methoxy, 16-substitued compounds. It is unclear to the Examiner what R is in Table 2 Page 33). Examiner could not find R in *any* of the structures throughout the specifications or the amended claims. A clarification is requested.

Specification discloses 16-modified analogs presented in Table 2 have significantly less estrogenic activity (compared to estradiol).

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The most active compound in this series as disclosed is 16alpha methyl compopund which has a greater activity than 2-methoxy estradiol when no methyl is at 16-position. (See line 12-13 on page 33. However, the IC50 disclosed shows no actual number but <0.5. The IC50 of known methoxy estradiol is 0.5. It is unclear what is the actual difference. Is the difference in the expected range?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 39, 12 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Entere Med, 2Me2-Non-confidential Overview, Angiogenesis Company, Updated 7/11/00 and Attala et al. (Biomedical and Biophysical Research Communication 228, 467-473 (1996). The references teach the method of inhibiting angiogenesis by 2-methoxy estradiol. See especially page 6 of the article from Angiogenesis Company.

The prior art of record is drawn to structurally similar compounds, which differ, from the compounds embraced by the instant claims in that they are homologues, i.e. H vs. Me or Et at 16-position. The skilled artisan would have been motivated to modify the teaching of the prior art to prepare homologues because it is recognized in the art that homologues are structurally similar and would be expected to possess similar properties. *Ex parte Henze* (POBA 1948) 83 USPQ 167.

Compounds that differ only by the presence of an extra methyl group are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders prima facie obvious its homologue.

The homologue is expected to be prepared by the same method and to have the same properties. This expectation is then deemed the motivation for preparing homologues. See *In re Wood* 199 USPQ 137; *In re Hoke* 195 USPQ 148; *In re Lohr* 137 USPQ 548; *In re Magerlein* 202 USPQ 473; *In re Wiechert* 152 USPQ 249; *Ex parte Henkel* 130 USPQ 474; *In re Fauque* 121 USPQ 425; *In re Druey* 138 USPQ 39.

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In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Allowable Subject Matter

2. Claims 14-16 and 18 are allowed. Prior art of record does not teach nor fairly suggests the steroids of formula in claim 1 when 16-position is substituted by Rh1 and Rh2 by n-Pr, I-Bu, CH₂OH, n-Bu, Me, or (CH₂)_n N(Me)₂ wherein n is from 1 to 6 and provided that Rh1 and Rh2 are not H.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is (571) 272-0622. The examiner can normally be reached on any business day.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Monday, 29 November, 2004



SABIHA QAZI, PH.D
PRIMARY EXAMINER